REMARKS

Claims 1 and 4 are pending in the subject application. Applicants have herein amended claim 4 as shown in **Exhibit B**. This amendment does not involve any issue of new matter. Support for this amendment may be found inter alia in the specification on page 10, lines 2-3 and 15-17. Therefore, entry of this amendment is respectfully requested such that claims 1 and 4 will be pending..

Status of priority applications

The Examiner stated that this application is a continuation application of Serial No. 08/763,669, now U.S. Patent No. 5,976,876, which has priority to provisional application 60/008,502. The Examiner stated applicant should amend the first line of the specification to include to current status of the non-provisional parent application and the correct numbering of the provisional priority document.

In response, applicants have hereinabove amended the specification to update the status of the priority applications. Applicants contend that this amendment obviates the above objection and respectfully request that the Examiner reconsider and withdraw this ground of objection.

Claim 4

The Examiner stated the disclosure is objected to because in claim 4 the term "competitively" is misspelled. The Examiner stated appropriate correction is required.

In response, applicants have hereinabove amended claim 4 such that it recites the term "competitively." Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejected claim 2 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner stated claim 2 would be more clear if it recited "an anti-hLHβcf antibody which competitively inhibits the binding of the antibody of claim 1 to *the human luteinizing hormone beta core fragment*."

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 4 in accordance with the Examiner's suggestions. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 1 and 4 under 35 U.S.C. §103(a) as being unpatentable over O'Connor et al. (Endocrine Reviews 15(6):650-683, 1994) in view of Campbell (Monoclonal Antibody Technology, Elsevier Sci. Publishing, 1984).

The Examiner stated that O'Connor et al. teach that human choricnic gonadotropin (hCG), in particular the β core fragment (hCGβcf), derived from the hCGβ subunit is a useful indicator in testing for pregnancy and many malignancies (see page 650, column 2 in particular). The Examiner stated that O'Connor et al. teach that the human luteinizing hormone (hLH) and hCG share extensive structural homology making immunoassays difficult because of the extensive cross-reactivity (see page 654, column 2; page 657, column 2 to page 658, column 1 in particular.). The Examiner stated that in addition, O'Connor et al. teach that structurally homologous fragments of the β subunits of both hLH (hLHβcf) and hCG (hCGβcf), or β-core fragments, which also show extensive cross-reactivity, have been identified in the urine (see page 654, column 2 in particular). The Examiner stated O'Connor et al. teach that the hCG and hLH cross-reactivity problems exist with polyclonal antisera, even when raised against the best available preparations of hCG or its β subunit and have caused investigators to turn to the production of monoclonal antibodies to prevent cross-reactivity in immunoassays since monoclonal antibodies can be screened for specificity to closely related antigens (see page 658, in particular). The Examiner stated that O'Connor et al. also teach antibodies which can completely inhibit the binding of the hCG-specific antibodies to its antigen to determine the relative orientation and location of the antibody binding domains (see page 661 in particular).

The Examiner stated that O'Connor does not teach the antibody which specifically binds to hLHβcf without cross reacting with hLH, hLHβ or hCGβcf. The Examiner stated however Campbell teaches that "[i]t is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)" (page 29, section on Basic Research in particular). The Examiner stated that Campbell also notes that one of the major advantages of monoclonal antibodies for diagnostic use is their high specificity which adds greatly to the accuracy and speed of the diagnosis (see pages 17-18, section on "Diagnostic Uses" in particular).

The Examiner stated therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to make antibodies specific for the hLHβ or hCGβcf and to also make antibodies that compete for binding to the same antigen as the hLHβcf-specific antibody. The Examiner stated that one having ordinary skill in the art would have been motivated to generate to mAbs specific to hLHβcf, one of the macromolecules under study as taught by Campbell, which do not cross react with hLH, hLHβ or hCGβcf because these fragments, which are found in the urine, are highly homologous and show extensive cross-reactivity as taught by O'Connor et al. The Examiner stated one having ordinary skill in the relevant art at the time the invention was made would be inclined to generate such hLHβcf-specific antibodies to

properly evaluate the levels of the newly isolated hLHβcf in immunoassays of urine samples without interference from structurally similar molecules such as hLH, hLHβcr hCGβcf as taught by O'Connor et al. The Examiner stated that one would further have been motivated to generate antibodies which competitively bind to the same antigen as the hLHβcf-specific antibody to assist in eptiope determination. The Examiner stated one skilled in the art at the time the invention was made would have had a reasonable expectation of success in generating the highly specific hLHβcf antibodies since the generation and screening of epitope-specific monoclonal antibodies is routine in the art and adds specificity, speed and accuracy in diagnostic applications, as taught by Campbell, and is the preferred method given the extensive cross-reactivity of the hCG and hLH glycoproteins as taught by O'Connor.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that the cited references, namely O'Connor et al. In view of Campbell do not render obvious the claimed invention.

First, the Examiner acknowledges that "O'Connor does not teach the antibody which specifically binds to hLHcf without cross reacting with hLH, hLHβ or hCGβcf." Accordingly, there is no disclosure in the primary reference of the invention of claim 1, i.e. an "antibody which specifically binds to human luteinizing hormone beta core fragment, (hLHβcf) without cross-reacting with human

luteinizing hormone (hLH), human luteinizing hormone free beta subunit (hLHβ) or human chorionic gonadotropin beta core fragment (hCGβcf)." In fact, applicants point out that the primary reference (O'Connor et al.) does not teach, suggest or disclose **human luteinizing hormone free beta subunit** or **hLHβ**, which is an element of the claim 1 which recites in part "...without cross reacting with human luteinizing hormone free beta subunit(hLHβ)..." [emphasis added]. In particular, applicants respectfully direct the Examiner's attention to Table 3 on page 657 of O'Connor et al. which discloses many immunogens, but not human luteinizing hormone free beta subunit or hLHβ. The secondary reference, i.e. Campbell, is merely a general discussion of properties and applications monoclonal antibodies. Campbell does not teach, suggest or disclose human luteinizing hormone free beta subunit or hLHβ, and therefore does not supply what is missing from the O'Connor et al. primary reference. Since O'Connor et al. do not disclose human luteinizing hormone free beta subunit(hLHβ), then it cannot teach, suggest or disclose an antibody which does not cross react with it. Moreover, O'Connor et al. state at page 658, column 2, that "[p]roducing monoclonal antibodies specific for hCG as compared to the highly homologous hormone hLH has not been a straightforward process. Accordingly, even if human luteinizing hormone free beta subunit or hLHβ had been disclosed in O'Connor et al. (which it was not), there would not have been a reasonable expectation of success in making the claimed antibody since O'Connor et al. indicates that it is difficult to make antibodies specific for one molecule but not the other, such as hCG but not hLH. Accordingly, the cited

references alone or in combination do not render obvious the claimed invention. Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Obviousness-type Double Patenting

The Examiner rejected claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,976,876. The Examiner stated that although the conflicting claim is not identical, it is not patentably distinct because the instant claim recites an antibody which specifically binds to hLHβcf without cross-reacting with hLH, hLHβ or hCGβcf. The Examiner stated that the antibody recited in Claim 1 of the '876 patent has the same binding activities as is a species within the genus of the instant claim 1. The Examiner stated that therefore, the patented claim is encompassed by the instant claim 1.

In response, applicants will soon forward a terminal disclaimer.

Summary

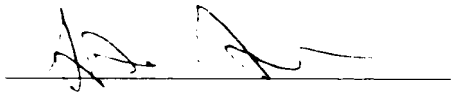
For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection set forth in the September 13,

2000 Office Action and earnestly solicit allowance of the now pending claims, i.e. claims 1 and 4 as amended.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone either of them at the number provided below.

No fee, other than the enclosed $445.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

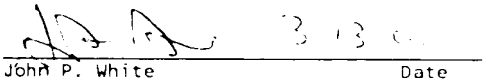

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EXHIBIT A

Page 1, lines 4-7

This application is a continuation of U.S. Serial No. 08/763,669, filed December 11, 1996, now U.S. Patent No. 5,976,876, issued November 2, 1999, which claims priority of U.S. Provisional Application No. [08/008,502] 60/008,502, filed December 11, 1995, the contents of which [is hereby incorporated into this application by reference] are hereby incorporated by reference into this application.

EXHIBIT B

--4. (2X Amended) An anti-hLH,cf antibody which [completitively] competitively inhibits [the] binding of the antibody of claim 1 to human luteinizing hormone beta core fragment.--